Kindly enter the following Amendment:

In the Claims:

Please add the following new claim:

--83. The purified or isolated ICAM-1 preparation as claimed in claim 71, wherein said purified or isolated ICAM-1 can bind p150,95.--

Remarks

Reconsideration of this Application is respectfully requested. In this amendment, Applicants have added new claim 83. New claim 83 corresponds to amended claim 74, which was inadvertently canceled in Applicants' Amendment and Reply Under 37 C.F.R. § 1.116. Claim 74 was filed on January 7, 1997, in Applicants' Amendment and Response to Restriction Requirement, and was entered and examined by the Examiner. Applicants respectfully request that the Examiner re-enter claim 74 as new claim 83. Thus, no new matter has been added by this amendment.

Upon entry of the foregoing amendment, claims 71-73, 75-78 and 80-83 are pending in the application, with claims 71 and 80 being the independent claims.

Rejections under 35 U.S.C. § 112

Claim 71 was rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to describe so as to enable ICAM-1 having amino acid sequences other than the sequence of Fig. 8. (Paper No. 17, § 4, at page 2.) According to the Examiner, "[o]ne with skill in the art would reasonably expect some minor allelic variants of the ICAM-1 sequence, e.g. due to somatic mutation. However, the instant specification does not explicitly describe by complete amino acid sequence any other allelic variant of the sequence of Fig. 8 . . . ." (*Id.* at page 3.)

Applicants' invention as presently claimed relates, *inter alia*, to a purified or isolated ICAM-1 preparation derived from a human source. The Examiner agreed that one with skill in the art would reasonably expect some minor allelic variants of the ICAM-1 sequence, e.g., due to somatic mutation. Thus, one of ordinary skill in the art would understand that a purified and isolated ICAM-1 preparation can comprise minor allelic variants of ICAM-1.

The Examiner, however, alleged that the specification does not describe by complete amino acid sequence any other allelic variant of the sequence of Fig. 8. Applicants submit that one of ordinary skill in the art would understand that the purified or isolated ICAM-1 preparation of claim 71 contains an ICAM-1 polypeptide derived from human cells or tissues that would have an amino acid sequence substantially similar to that shown in Fig. 8. The Examiner has not established that any other allelic variant of ICAM-1 can be derived from human cells or tissues. Moreover, Applicants need not disclose every species encompassed by a claim to satisfy the requirements of 35 U.S.C. § 112. *In re Angstadt*, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection.

Claims 80-82 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly "lacking adequate description in the specification as filed for an 'artificial membrane comprising purified

or isolated ICAM-1' that is capable of binding to LFA-1, Mac-1 or p150,95." (Paper No. 17, § 6, at page 3.) Applicants respectfully traverse this rejection.

Applicants submit that the specification adequately describes an artificial membrane comprising purified or isolated ICAM-1 that is capable of binding to LFA-1. At pages 85-89 of the specification, Applicants describe reconstituting purified ICAM-1 into artificial lipid membranes and assaying the binding of cells that are LFA-1 positive and cells that are LFA-1 deficient. The results indicate that only cells expressing LFA-1 bind to purified ICAM-1 incorporated into the artificial lipid membranes (*see* Figures 11 and 12). This establishes that ICAM-1 can bind LFA-1, when the ICAM-1 is inserted into artificial lipid membranes. Thus, the specification as filed more than adequately describes the detailed methodology and functional characterization of purified ICAM-1 incorporated into artificial lipid membranes. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection.

Rejections under 35 U.S.C. § 102

The Examiner rejected claims 71-73 under 35 U.S.C. § 102(b) as allegedly being anticipated by Tomassini, thesis 8624033 (1986) [hereinafter "the Tomassini thesis"], or Tomassini *et al.*, *J. Virol. 58*:290-295 (1986) [hereinafter "the Tomassini article"]. The Examiner indicated that Applicants' argument was not persuasive because "poor binding of radio labeled HRV is more likely to be attributable to chemical denaturation and subsequent disruption of the binding sites on the virus (not HRRP or ICAM-1) by radio labeling protocols." (Paper No. 17, § 7, at page 4.) Applicants respectfully traverse this ground for rejection.

In the Tomassini thesis and article, the authors indicate that "[r]epeated attempts to use radiolabeled HRV in place of receptor antibody in the RIA gave inconclusive results owing to

poor virus binding." (Tomassini thesis at 44, lines 9-12; and Tomassini article at 292, col. 2, lines 18-21.) The authors further indicate that "it is quite tempting to speculate that a pentamer of the 90-kDa receptor protein is needed for a functional receptor complex. This would correlate well with the 440-kDa receptor peak obtained by gel filtration and the inability to isolate a 90-kDa receptor protein capable of binding virus." (Tomassini thesis at 116, line 22, to 117, line 1; and Tomassini article at 295, col. 1, lines 20-25.) Thus, in the authors' opinion, the poor binding of the HRRP receptor to virus is not due to "chemical denaturation and subsequent disruption of the binding sites on the virus by radio labeling protocols," but rather due to the fact that the purified HRRP (ICAM-1) receptor preparation relied on by the Examiner is not able to bind HRV. Thus, the purification procedures taught in the Tomassini thesis and Tomassini article appear to disrupt the HRRP receptor structure such that HRV binding is eliminated. Since the binding sites for HRV and LFA-1 overlap, one of ordinary skill in the art would expect that any disruption in structure from the purification procedure leading to the elimination of HRV binding, would also reduce or eliminate LFA-1 binding. Therefore, one of ordinary skill in the art would not expect that the HRRP preparation of Tomassini would exhibit the ability to bind ligands as recited in the pending claims. The Tomassini HRRP preparation, consequently, cannot anticipate the presently pending claims.

As to the Examiner's argument that poor binding of radio labeled HRV is more likely to be attributable to chemical denaturation and subsequent disruption of the binding sites on the virus (not HRRP or ICAM-1) by radio labeling protocols, Applicants respectfully point out the following. The Tomassini article teaches the inhibition of radio labeled HRV binding by polyclonal rabbit antibodies in membrane binding and cell protection assays. (Tomassini article at 293, col. 2, lines 10-16; Figure 4; and Table 1.) The results showed that the addition of

increasing amounts of receptor antiserum corresponded to an increased inhibition of ^{35}S-labeled HRV binding to HeLa membranes. No inhibition of virus binding was observed with dilutions of control antiserum. (*Id.* at 293, col. 2, line 16, to 294, col. 1, line 4.) These results indicate that radio labeled HRV was capable of binding to membranes, demonstrating that the binding sites on radio labeled HRV are not denatured or disrupted by the radio labeling protocols, but are functional. Since radio labeled HRV binds membranes but does not bind to Tomassini's HRRP preparation, Applicants' interpretation of the Tomassini article is more consistent with the experimental results, than the interpretation the Examiner has adopted.

The Examiner also rejected claims 80-82 under 35 U.S.C. § 102(b) as allegedly being anticipated by Tomassini, thesis 8624033 (1986), or Tomassini *et al.*, *J. Virol. 58*:290-295 (1986). (Paper No. 17, § 9, at page 6.) The Examiner stated that "[t]he remaining issue is whether HRRP or ICAM-1 when associated with detergents, such as in micellar form, would be considered an artificial lipid membrane." *Id.*

Applicants respectfully contend that it is irrelevant whether HRRP or ICAM-1 when associated with detergents, such as in micellar form, would be considered an artificial lipid membrane. As discussed *supra* in response to the previous rejection, the Tomassini thesis and the Tomassini article do not teach the isolation of HRRP in active form as presently claimed. Thus, one of ordinary skill in the art would not have reason to expect that Tomassini's HRRP or ICAM-1 preparation, when associated with detergents, is functional. In contrast, Applicants describe, at pages 85-89 of the specification, reconstituting purified ICAM-1 into artificial lipid membranes and assaying the binding of cells that are LFA-1 positive and cells that are LFA-1 deficient. The results indicate that only cells expressing LFA-1 bind to purified ICAM-1 incorporated into the artificial lipid membranes (*see* Figures 11 and 12). Thus, one of ordinary

skill in the art would understand that ICAM-1 incorporated into Applicants' artificial lipid membranes is functional. Since Applicants' ICAM-1 preparation is functional as compared to Tomassini's ICAM-1 preparation, which is not functional, claims 80-82 are not anticipated by Tomassini. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

Rejections under 35 U.S.C. § 103

Claims 71-73 and 75-78 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Tomassini, thesis 8624033 (1986) or Tomassini *et al.*, *J. Virol. 58*:290-295 (1986). (Paper No. 17, § 8, at page 5.) It is the Examiner's opinion that "the HRV receptor is ubiquitous in the human body, and thus one with ordinary skill in the art at the time of invention would have had a reasonable expectation of isolating HRRP (ICAM-1) from any tissue in the human body . . . ." *Id.* Applicants respectfully traverse this rejection.

Claim 71, from which claims 72-73 and 75-78 depend, is directed to a "purified or isolated ICAM-1 preparation . . . capable of binding to LFA-1, Mac-1, or p150,95. Applicants contend that one with ordinary skill in the art would not have had reason to expect that their ICAM-1 purification procedure would yield ICAM-1 capable of binding to LFA-1, Mac-1, or p150,95. In fact, the authors of the Tomassini thesis and the Tomassini article indicate that they are unable to isolate a 90-kDa receptor protein capable of binding virus. Thus, based on the teachings of the Tomassini thesis and the Tomassini article, and the fact that the binding sites for LFA-1 and HRV overlap, one of ordinary skill in the art would have no reason to believe that purified HRRP (ICAM-1) would bind to LFA-1, Mac-1, or p150,95. Therefore, the Tomassini thesis and the Tomassini article do not teach the isolation of HRRP in active form as presently claimed. No

other art has been cited by the Examiner to establish the purification of HRRP in an active form. Therefore, the Examiner has failed to establish a *prima facie* case of obviousness, and Applicants respectfully request that this ground for rejection be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. It is believed that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment is respectfully requested.

Respectfully submitted,

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